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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,783	12/06/2006	Katiuscia Arrighi	290242US0PCT	8685
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OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314			EXAMINER CUTLIFF, YATE KAI RENE	
			ART UNIT	PAPER NUMBER
			1621	
			NOTIFICATION DATE	DELIVERY MODE
			05/30/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/578,783	Applicant(s) ARRIGHI ET AL.	
	Examiner YATE K. CUTLIFF	Art Unit 1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.
2. The finality of the Office Action of March 7, 2008 is withdrawn in view of the new ground of rejection as set forth below.
3. The indicated allowability of claim 26 and 27 is withdrawn in view of the new ground of rejection as set out below.

Response to Amendment

4. The amendments to claims 1, 9 and 15 have been entered.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

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the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-25 rejected under 35 U.S.C. 103(a) as being unpatentable over Fan W. et al. (CN 1297885) in view of Bromine Compounds, Ltd. (Bromine) (WO 03/002517), and further in view of Shavel, Jr. et al. (US 3,007,940).

9. Rejected claims 1 and 15 teaches the process for the preparation of 1,1-cyclohexanediacetic acid monoamide (acid monoamide or CHDAAM), which comprises:
a) the amination of 1, 1-cyclohexanediacetic acid anhydride by reaction with aqueous NH_3 at a temperature lower than 30°C by using a NH_3 /anhydride molar ratio lower than 3; b) the product precipitation through the acidification of the reaction mixture, wherein the 1,1- cyclohexanediacetic acid monoamide is not crystallized.

Rejected claims 2, 3, 16, and 17 teach that the NH_3 is in aqueous solutions of various concentration amounts. Rejected claims 4 and 18 teach the use of hydrochloric acid in the acidification step, while rejected claims 5 and 19 teach the concentration amount. Rejected claims 6, 7, 20 and 21 teach the molar ratios for ammonia to 1,1-cyclohexanediacetic acid anhydride. Rejected claims 8 and 22 teach the reaction temperature.

Rejected claim 9 teaches a precipitation process of 1,1-cyclohexanediamic acid monoamide by acidification of the ammoniacal solution of the monoamide and where the 1,1-cyclohexanediamic acid monoamide is not crystallized. Rejected claim 10 disclosed the use of hydrochloric acid in the gaseous form, while rejected claim 11 teaches the concentration of the hydrochloric acid.

Rejected claims 12, 13, 14, 23, 24 and 25 teach a process for transforming 1,1-cyclohexanediamic acid into the corresponding anhydride, with or without the presence of an organic solvent.

Fan et al. teaches discloses a process for preparing 1,1-cyclohexanediamic acid monoamide by amination of 1,1-cyclohexanediamic acid anhydride at a temperature of 30-110°C. The process of Fan discloses the use of an organic solvent (methylbenzene) in its process of forming the acid monoamide. Additionally, Fan et al. teaches a molar ratio of 2.2-4, which is within the claimed molar ratio of lower than 3.

Bromine, on page 2 discloses a reaction that produces 1,1-cyclohexanediamic acid monoamide by amination with ammonia in an aqueous solution, than the acidification of the reaction product with hydrochloric acid. Bromine teaches the same type of reaction where the reaction temperature is below 20°C, however, the NH_3 /anhydride molar ratio is 5 to 10. (see page 3 paragraph 5). Additionally, neutralization (acidification to precipitate the 1,1-cyclohexanediamic acid monoamide) is carried out with H_2SO_4 and at a temperature below 30°C. (see page 5 paragraph 4). However, on page 4 of Bromine discloses that neutralization of the reaction mixture can be carried out with aqueous hydrochloric acid, and the acid

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monoamide precipitates when the solution is slightly acid. Further, according to Bromine the crystallization step is simply done to further purify the crude CHDAAM and thus not necessary. (see page 6, line 5). In Bromine, prior to purification by crystallization, the crude CHDAAM resulting from the neutralizations stage is water washed to separate it from the slurry generated. (see page 6, 1st paragraph).

Shavel, Jr., in Example 1 at column 4, teaches the process for making cyclohexanediacetic anhydride from cyclohexanediacetic acid in a reaction with acetic anhydride without an organic solvent.

The difference between the claimed invention and main references of Fan et al. and Bromine is the temperature and the molar ratio of NH_3 /anhydride; and the inclusion of a crystallization step to purify the crude 1,1-cyclohexanediacetic acid monoamide.

However, change in temperature, concentration, or both, is not a patentable modification unless such changes produce new and unexpected result which is different in kind and not merely in degree from results of prior art. It is known from the disclosure of Fan et al. that a molar ratio lower than 3 has a positive affect in optimizing the yield of 1,1-cyclohexyl oxalic amide in the reaction. The skilled artisan would be motivated to change a result-effective variable. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233, 235 (CCPA 1955).

In this instance, both prior art references aminate 1,1-cyclohexanediacetic acid anhydride with NH_3 . The variations in temperature and molar variations are merely an

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optimization of range or other variable within the claims that flow from "normal desire of artisan to improve upon what is already known. Further, there is no evidence to indicate the claimed process obtains a greater purity than obtained by Bromine. Therefore, any chemist reading the prior art could logically assume that higher purity might be obtainable, and by experimentally varying the conditions of temperature and acidity could find the most productive conditions.

With regard to use of crystallization by both Fan and Bromine as an additional purification process, it is noted in Bromine that the process, as discussed, is not necessary. Both Bromine and Applicant water wash the crude CHDAAM precipitate of neutralization (with acid). The water washing by Applicant, would be understood by one skilled in the art can be deemed as a different means of further purification of Applicant's crude acid monoamide. Applicant's process merely eliminates the additional purification step of crystallization of the crude acid monoamide, when by Applicant's own admission high purity is not required for transformation of the 1,1-cyclohexanediamic acid monoamide for production of gabapentin. Omission of an element and its function is obvious if the function of the element is not desired. *Ex parte* Wu, 10 USPQ 2031 (Bd. Pat. App. & Inter. 1989). MPEP 2144.04

One of ordinary skill in the art would have been motivated to eliminate the additional crystallization step from the preparation of the 1,1-cyclohexanediamic acid monoamide because of the high yields and high purity asserted by Bromine and Fan et al. are not desired in an industrial production process for gabapentin. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the

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time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to YATE K. CUTLIFF whose telephone number is (571)272-9067. The examiner can normally be reached on M-TH 8:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (571) 272 - 0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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